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MORPHOLOGICAL STUDIES OF THE VESTIBULAR NERVE

by

Björn Bergström

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This summary is based on the following papers, which will be referred to by the Roman numerals I—IV.

I. Bergström, B. 1973. Morphology of the vestibular nerve: I. Anatomical studies of the vestibular nerve in man. *Acta Otolaryng (Stockh.)*. In press.

II. Bergström, B. 1973. Morphology of the vestibular nerve: II. The number of myelinated vestibular nerve fibers in man at various ages. *Acta Otolaryng (Stockh.)*. In press.

III. Bergström, B. 1973. Morphology of the vestibular nerve: III. Analysis of the calibers of the myelinated vestibular nerve fibers in man at various ages. *Acta Otolaryng (Stockh.)*. In press.

IV. Engström, H., Bergström, B., and Ades, H.W. 1972. Macula utriculi and macula sacculi in the squirrel monkey. *Acta Otolaryng (Stockh.)*. Suppl. 301, 75—126.

A. INTRODUCTION

During the last decades microsurgery of the temporal bone has come to play an increasingly important role. Methods and instruments have been developed that make possible operations on branches of the facial and vestibulocochlear nerves and the inner ear without damaging adjacent structures. The exposure of man and experimental animals to very high or very low G-forces during certain stages of space flights have also led to an augmented interest in vestibular function and structure. As a consequence there is an increasing demand for precise knowledge of the structures in this area such as nerves, blood vessels and sensory regions. With these aspects in mind the following subjects have been included in the present study:

I. A study of the anatomy of the vestibular nerve in man with a survey of the literature concerning the peripheral vestibular system. This study includes a description of the topographical anatomy of the VIIIth cranial nerve in man with its relations to the inner ear and the facial nerve. It also contains a light microscopic study of the vestibular nerve branches and the vestibular ganglion.

II. Against this background it was natural to proceed the project with studies of possible age related degenerative changes in the vestibular nerve — a controversial question for many years. Since none of the earlier reports in this field was based on numerical studies it seemed essential to carry out a numerical study of the vestibular nerve and its branches to ascertain: a) what might be termed the "normal" number of nerve fibers and b) whether any reduction in number occurs with increasing age.

III. Based on the observations in part II that there is an age related modification of the vestibular nerve the caliber spectra of the myelinated vestibular nerve fibers have been analysed in order to determine the distribution of thick and thin fibers in the ampullary and macular branches at various ages.

IV. To acquire an understanding of the peripheral course of the vestibular nerve fibers the neuroanatomical studies have been extended down to the ultrastructural level. The vestibular sensory cells and their innervation have

been the subject of an extensive electron microscopic study which was done on the squirrel monkey.

The light microscopic and electron microscopic findings in these studies have been correlated to each other.

B. SURVEY OF LITERATURE

1. Topographic and gross anatomy of the peripheral vestibular system

The anatomy of the vestibular nerve has been studied by several authors. Many species of mammals including man have been investigated and found to have great structural similarities (Retzius, 1884; Voit, 1907; Lorente de Nó, 1926; Shute, 1951; Anson *et al.*, 1967; Gacek, 1969; Sando *et al.*, 1972 and others).

The VIIIth cranial nerve (n vestibulocochlearis) contains the afferent fibers from the sensory regions of the inner ear to the vestibular and cochlear nuclei in the brain stem. It also contains efferent fibers to the cochlea (Rasmussen, 1942, 1946) and to the vestibular end organs (Petroff, 1955; Rasmussen and Gacek, 1958; Gacek, 1960, 1966) as well as adrenergic fibers (Spoendlin and Lichtensteiger, 1966; Ross, 1971).

According to the Nomina Anatomica (1968) the vestibulocochlear nerve is divided in two main portions, pars vestibularis and pars cochlearis. Pars vestibularis consists of the vestibular nerve except the saccular nerve branch which by the Nomina Anatomica is separated as a special nerve. No explanation is given why this branch of the vestibular nerve is considered a separate nerve. There are no indications in modern literature or in the present investigation that the saccular nerve is not a portion of the vestibular nerve.

The vestibulocochlear nerve leaves the brain stem laterally in the cerebello-pontine angle immediately below the lower border of pons. Together with the facial nerve it goes through the internal acoustic porus into the internal auditory meatus. The nerves are surrounded by a common dural sheath. The facial nerve is positioned antero-superiorly with the vestibulocochlear nerve below and behind (Fig. 1). The fundus region of the internal meatus is divided in two halves by a bone ridge, the transverse crest. Laterally in the internal auditory meatus the nerves separate; the facial nerve continues in its own bony canal while the cochlear nerve with its spirally turned ganglion in the modiolus goes on to the organ of Corti. The vestibular nerve divides into one superior and one inferior division. The superior division passes with the facial nerve over the transverse crest and the inferior division runs with the cochlear nerve under the crest. The vestibular ganglion is situated at the bottom of the internal meatus. Two main portions of the ganglion can be distinguished, pars superior and

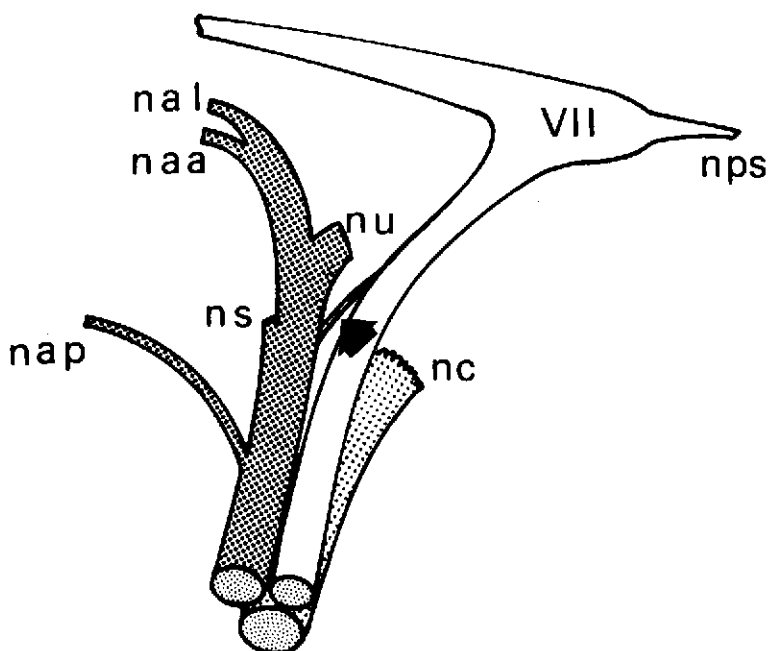


Fig. 1. Schematic drawing of the vestibulocochlear and facial nerves seen from the superomedial side. "VII" facial nerve. "nc" cochlear nerve. "naa" anterior ampullary nerve. "nal" lateral ampullary nerve. "nap" posterior ampullary nerve. "ns" saccular nerve. "nu" utricular nerve. "nps" superficial petrosal nerves. Arrow indicates vestibulofacial anastomosis.

inferior, they are connected by the isthmus ganglionaris (Alexander, 1899). The superior division of the vestibular nerve innervates the sensory epithelia of the lateral and anterior cristae ampullares and the macula utriculi plus a small portion of the macula sacculi while the inferior division innervates the main part of the macula sacculi and the posterior ampullary crista.

That a small part of the macula sacculi is innervated by the superior division of the vestibular nerve was first observed by Retzius (1881) in teleosts and by Voit (1907) in different species of mammals. The small nerve is usually called Voit's nerve or anastomosis. In mammals including man there is a connection between the inferior division of the vestibular nerve and the cochlear nerve, the vestibulocochlear anastomosis (Oort, 1918). It consists of efferent (Rasmussen, 1946) and afferent (Rasmussen, 1953)

fibers to the cochlea. A connection between the lateral ampullary nerve and the utricular nerve was described by Shute (1951); it was thought to contribute to the innervation of the macula utriculi. Lorente de Nó (1926) described an anastomosis between the facial nerve and the VIIIth nerve. These fibers were shown to leave the facial nerve at the level of the proximal part of the geniculate ganglion (Shute, 1951). An anastomosis between the vestibular and facial nerves carries fibers belonging to the intermedius nerve (Gacek and Rasmussen, 1961).

2. The vestibular sensory epithelium

a) Structure of the sensory cells

The sensory epithelia on the ampullary cristae and the maculae consist of hair cells and supporting cells. The hair cells have one long kinocilium and several stereocilia arranged in a characteristic pattern. Wersäll (1956) described two types of hair cells, type I who were bottle shaped and surrounded by a nerve calyx that almost enclosed the whole cell, and type II cells that were more cylindrical and were innervated by nerve fibers with bouton shaped nerve endings. The type I cells were mostly seen on top of the crista while the type II cells were predominantly found in the periphery. In the guinea pig Lindeman (1969) found a relation of approximately 3:2 between type I and type II cells all over the surface of the crista. Watanuki and Meyer zum Gottesberge (1971) employed different techniques and found the distribution to be 45 % type I and 55 % type II cells both on top of the crista and in the periphery.

On the maculae a lighter zone, the striola (Werner, 1933) can be seen even at a low magnification in the for the rest homogenous sensory epithelium. According to Lindeman (1969) the striola is the central, curved area where the sensory epithelium and the statoconial membrane have a characteristic structure (Fig. 2). The hair cells in this area have a much larger free surface than the cells outside the striola. Type I cells dominate in the striola while in the peripheral areas there are about as many type I as type II cells according to Lindeman. Watanuki *et al.* (1971) also found that type I cells dominate in the striola but type II cells are so numerous in the periphery that they outnumber the type I cells on the macula. They found 1.2 times more type II than type I cells on the macula sacculi and 1.1 times more on the macula utriculi.

The hair cells on the cristae are covered by a gelatinous mass, the cupula,

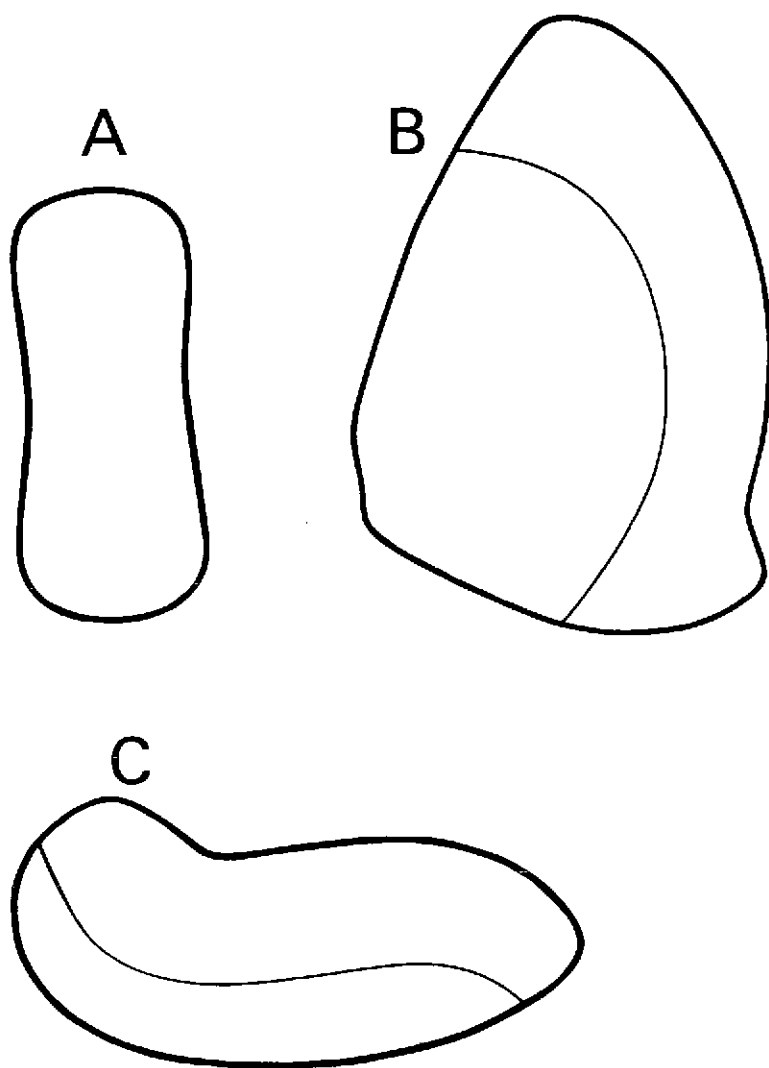


Fig. 2. Schematic drawings of A) crista ampullaris, B) macula utriculi and C) macula sacculi.

into which the hairs penetrate. On the maculae this mass contains a great number of hexagonal, elongated calcite crystals, statoconiae which are densely packed in several layers, the statoconial membrane. Sasaki (1970), however, is of the opinion that these crystals are postmortal artifacts and that during life they have a diameter of only 0.1μ .

b) Morphological polarization

The hair cells on the cristae are all orientated in a certain direction, i.e. the kinocilium is localized in the same direction on all cells. The hair cells are said to be morphologically polarized in a certain direction. It has been shown that there is a specific pattern for this polarization. On the crista of the lateral ampulla the cells are polarized towards the utricle while on the cristae of the two vertical ampullae the polarization is directed from the utricle (Lowenstein and Wersäll, 1959; Wersäll, 1961). On the macula utriculi the hair cells are polarized towards the striola and on the macula sacculi away from the striola (Engström *et al.*, 1962; Flock, 1964; Spoendlin, 1964, 1965; Lindeman, 1969).

The macula utriculi is almost kidney shaped, the anterior part is often slightly broader than the posterior. In the normal anatomical position, i.e. in man the erect position with the head bent 30° forwards the sensory epithelium lies with its main plane horizontally and the anterior tip slightly elevated. Thus the hair cells become polarized posteriorly, laterally, medially and in the anterior part, also superiorly and inferiorly.

The macula sacculi is shaped rather like a hook with the anterior part of the epithelium bulging outwards in a superior direction. In the normal anatomical position the macula sacculi is orientated almost vertically with the antero-superior part so situated that the hair cells here face slightly inferiorly. The polarization will then be mainly in a postero-superior and antero-inferior direction (cf. Lindeman, 1969).

The three semicircular canals are principally positioned in definite planes at right angles to each other. In the normal anatomical position the lateral semicircular canal lies in the horizontal plane. The ampullary cristae are saddle shaped with the long axis vertical to the plane of the semicircular canal, although minor irregularities have been described (Retzius, 1884; Lindeman, 1969 and others). The sensory cells on the vertical cristae extend further down on the utricular than the canalicular side while on the lateral crista the cells are symmetrically distributed (Wersäll, 1956).

c) Functional polarization and physiological significance

The morphological polarization is accompanied by a functional polarization. An utriculo-petal deviation of the cupula on the lateral crista gives a depolarization of the sensory epithelium (Trincker, 1957) and an increased impulse frequency in the nerve fibers (Lowenstein and Sand, 1940). An utriculo-fugal deviation of the cupula gives a hyperpolarization and a decreased impulse frequency. The opposite conditions are at hand in the vertical cristae.

Gernandt (1949) isolated solitary functional units of the vestibular nerve in cat and studied those belonging to the lateral semicircular canal. He found 3 different types of response to rotation. In 83 % an increase of the action potentials was recorded at rotation towards the examined side and a decrease at rotation from the examined side. In 12 % of the cases there was an increase of the action potentials at rotation in both directions while in 5 % a decrease of the action potentials at rotation in both directions was observed.

Flock (1964) studied the macula utriculi in a teleost (*Lota vulgaris*) and concluded that there is a complicated pattern of interacting afferent and efferent impulses and that the morphological polarization of the hair cells decides their directional sensitivity.

Fluur (1970) made experiments with linear accelerations in different planes and studied the influence of the maculae on the oculo-motor system. He could also clarify the synergistic and antagonistic interrelationship between different regions of the maculae.

Fluur and Siegborn (1973) have investigated the interaction between the utricles and the horizontal canals. After selective sectioning of the left horizontal ampullary nerve they studied how changes in the utricular activity caused by tilting along the longitudinal axis of the animal influenced the destruction nystagmus.

Fernandez and coworkers found certain discharge characteristics of the peripheral afferents innervating the cristae and maculae of the squirrel monkey. They observed a resting discharge which was higher in the ampullary nerves (average 90 spikes/sec) than in the macular branches where the utricular nerve had a resting discharge of 79 spikes/sec on average and the saccular nerve only 47 spikes/sec. They also found that most neurons had a regular discharge pattern and in this group those who had the highest resting discharge were the most sensitive to stimuli. In neurons where the discharge was irregular, no such relation was apparent.

The irregular neurons included the most sensitive units of all neurons present. There were relatively fewer irregular units among the macular neurons than among those to the cristae. The authors suggested that the regular units correspond to the thin fibers innervating the type II cells and the irregular units correspond to the thick fibers to the type I cells. However, they considered the question unsettled until more unequivocal evidence could be obtained (Fernandez and Goldberg, 1971; Goldberg and Fernandez, 1971 a, 1971 b; Fernandez *et al.*, 1972).

3. The vestibular nerve

a) The afferent vestibular nerve fibers

The afferent vestibular nerve fibers are myelinated. Lindeman (1969) studied the peripheral distribution of the vestibular nerve fibers. The myelinated fibers to the cristae show a tendency to run in two branches, one on the canalicular and one on the utricular side. The utricular nerve fibers pass anteriorly and slightly medially under the sensory epithelium and spread out underneath it. The macula sacculi was found to be innervated mainly by the saccular nerve but the antero-superior portion was innervated by Voit's nerve. In the borderline region between the areas of innervation a distinct overlapping of fibers from the two nerve branches was found. This overlapping was said to be most pronounced in man.

Gacek (1969) and Sando *et al.* (1972) have determined and chartered the relationships of the afferent vestibular nerve fibers in the internal auditory meatus in the cat. At the distal end of the internal meatus the anterior ampullary nerve lies postero-superior to the lateral ampullary nerve. The utricular nerve is positioned inferior and posterior to the ampullary branches. These three branches constitute the superior division of the vestibular nerve and they lie above the transverse crest. The saccular nerve and the posterior ampullary nerve form the inferior division where the saccular nerve lies anterior and superior to the ampullary branch. These relationships are principally maintained during the course of the nerve fibers to the vestibular ganglion. Central to the ganglion the nerve branches change positions and at the level of the porus the posterior ampullary nerve lies immediately inferior to the superior ampullary nerves and superior to the macular branches, the utricular nerve anterior to the saccular.

According to Sando *et al.* (1972) the ampullary nerve fibers rotate in a clockwise direction and the macular fibers in a counterclockwise direction during their course in the meatus (right ear as seen from the medial side). The cochlear nerve lies inferior and anterior to the vestibular nerve at the transverse crest and the facial nerve anterior and superior to the vestibular nerve. At the level of the porus the vestibular and cochlear nerves have joined with the vestibular fibers anterosuperior to the cochlear and the facial nerve lies immediately anterior to the vestibular nerve.

The ampullary branches contain a high proportion of thick fibers. The thick fibers were found to be related to the top of the cristae and distally they run as a central core surrounded by the thinner fibers. The macular nerve fibers are mostly thin but a certain amount of thick fibers are scattered among these (Gacek, 1969).

b) The vestibular ganglion

1. Morphology of the vestibular ganglion

In the vestibular ganglion a connection between the ganglion cells of the superior and the inferior parts of the vestibular nerve was described by Alexander (1899) who called it the isthmus ganglionaris. Wersäll (1956) stated that the vestibular ganglion cells in the guinea pig were localized not only in the ganglion itself but also were scattered in the isthmus and the nerve branches. According to Ballantyne and Engström (1969), however, the ganglion cells in higher mammals form one ganglion only but a few ganglion cells can occasionally be seen at some distance from the ganglion. They also showed that the vestibular ganglion cells vary considerably in size and that with regard to diameters, there are at least two different populations of myelinated cells. There is one small group with an average diameter of about 23 μ and one large group with an average diameter of about 30 μ . Apart from the differences in diameter they also found that the cells were of different structure; the majority both large and small were myelinated but there were also unmyelinated cells. Most cells had a myelin sheath but there was a small number of cells, mostly small that were covered only by a simple layer of satellite cell cytoplasm. Those resembled very much the cells in the spiral ganglion earlier described by Kellerhals *et al.* (1967). The cytoplasm is more filamentous than in the myelinated cells and the endoplasmic reticulum is not so richly developed.

The myelin sheath of the myelinated cells extends along both dendrite and neurite. The appearance of the myelin sheath around the ganglion cell

can vary much in different regions and loose lamellae can change with dense even in the same region. The Schwann cell nucleus is often situated in a cytoplasmic out-pouching by the wall of the ganglion cell. The Schwann cells often contain very large mitochondria with densely packed cristae. The innermost myelin layers around the vestibular ganglion cell are often so irregular and distorted compared to the nerve fiber sheaths that they have a granular appearance. The myelinated ganglion cell is often ovoid or round and it has a nucleus in the center or peripherally.

2. Tonotopic organization in the vestibular ganglion

It has been much discussed whether a tonotopic organization exists between the sensory cells and the ganglion cells, i.e. that the functionally different areas of the sensory regions have determined projections in the vestibular ganglion as well as in the brain stem nuclei. Lorente de Nó (1926, 1931) divided the vestibular ganglion into five regions separated by the size of the ganglion cells. These regions were called *pars magnocellularis anterior*, *pars parvicellularis anterior*, *pars magnocellularis posterior (a)*, *pars magnocellularis posterior (b)* and *pars parvicellularis posterior*. Each region was shown to receive fibers from specific parts of the vestibular sensory regions.

Weston (1939) studied the vestibular ganglion in birds, reptiles and fish and could follow the fibers from the cristae to larger ganglion cells than those from the maculae.

Werner (1960) found large and small ganglion cells irregularly distributed in the vestibular ganglion in the guinea pig, rabbit and dog.

Gacek (1969) found the cat's vestibular ganglion to form a very compact, linearly arranged mass of cells which spread out in an antero-inferior direction. Also here a superior and an inferior part could be distinguished and they were related to the superior and inferior divisions of the vestibular nerve respectively. The ganglion cells related to the macula utriculi occupy the most antero-inferior part of the pars superior while the saccular ganglion cells are found in the saccular nerve anterior to the cells for the posterior crista and bordering to the cochlear nerve stem. The ganglion cells related to the anterior and lateral cristae are located partly anteriorly in the superior portion of the ganglion and partly postero-inferiorly immediately superior to the ganglion cells for the macula utriculi. Gacek found that the superior ampullary nerves receive about the same amount of fibers from

both these cell masses and as far as the ganglion is concerned it is one nerve which peripherally divides into two branches. In the vestibular nerve stem central to the vestibular ganglion the fibers from the cristae constitute the superior 2/3 of the nerve stem while the macular fibers constitute the inferior 1/3 according to Gacek.

In a study by Stein and Carpenter (1967) the neurites from the superior vestibular ganglion cells were found to form the superior 2/3 of the vestibular nerve stem with the ampullary fibers running above those from the macula utriculi. The inferior 1/3 of the vestibular nerve stem was composed by the neurites from the inferior ganglion cells with the fibers related to the posterior crista positioned superior to those of the macula sacculi.

c) Central distribution of vestibular nerve fibers

After entering the brain stem the neurites of the vestibular nerve divide in ascending and descending branches to reach contact with the vestibular nuclei in the bottom of the fourth ventricle. Apart from the four classical nuclei, nucleus superior, nucleus medialis, nucleus lateralis, and nucleus inferior there is also the interstitial nucleus of the vestibular nerve and a number of small cell groups called x, y and z.

Within each of the four classical nuclei are regions who do not receive primary vestibular fibers but for practical reasons it has been considered suitable to retain the accepted nomenclature especially as both "vestibular" and "non-vestibular" parts of the nuclei are very much alike in structure and other fiber connections. In accordance with this reasoning some minor cell groups have been included in the vestibular system even if they do not receive primary vestibular fibers. Regional cyto-architectonic differences in the nuclei suggest a functional differentiation which is also evident when the distribution of fibers to the nuclei is studied and it is also seen in physiological studies (cf. Brodal *et al.*, 1962).

There is also a central tonotopical organization so that different parts of the vestibular sensory regions are projected to separate parts of the vestibular nuclei. Stein and Carpenter (1967) found in their investigation on monkey that the neurites from those ganglion cells that innervate the ampullary cristae are mainly projected to portions of nucleus superior and to the superior parts of nucleus medialis. Central fibers related to the posterior crista were projected to the more medial and inferior parts of nucleus superior.

The neurites from the ganglion cells innervating the macula utriculi traverse, and give collaterals to, anterior parts of nucleus lateralis and reach down in the postero-medial part of nucleus inferior, collaterals from these descending fibers being projected to nucleus medialis. A small number of the descending fibers from the utricular part of the superior vestibular ganglion pass nucleus inferior and reach nucleus cuneatus accessorius.

The macula sacculi is projected to the postero-lateral parts of nucleus inferior.

Some vestibular ganglion cells are projected to portions of all four vestibular nuclei so that every special part of the labyrinth has one specific as well as a common projection in the vestibular nuclei. Primary vestibular fibers from all regions of the vestibular ganglion are projected to parts of the nucleus interstitialis.

According to Gacek (1969) the neurites from the ampullary cristae are connected with the nucleus interstitialis via short collaterals. After they have given off these collaterals the neurites continue into the brain stem where each axon divides into one ascending and one descending branch. The ascending branches have their nerve endings in nucleus superior and cerebellum while the descending branches run in the vestibular root and give off collaterals to nucleus lateralis, medialis and inferior. The neurites from the maculae have no connection with nucleus interstitialis or superior. The ascending branches of the utricular neurites have their nerve endings in the antero-superior part of the nucleus lateralis and in the superior part of nucleus medialis while the descending branches give off collaterals to the inferior part of nucleus medialis and the superior part of nucleus inferior. The nerve endings of the saccular neurites were said to be mainly localized to the group "y" nucleus with Brodal's nomenclature and to a lesser extent also to the nucleus lateralis and inferior. Earlier investigations have not been able to show any afferent fibers to group "y" (Brodal *et al.*, 1962).

The thick fibers from the two superior cristae were found to have their nerve endings in nucleus superior against the large cells in the center of the nucleus while the thinner fibers terminated in the periphery of the nucleus where small cells predominate. Gacek meant that these findings indicate different functional properties for the type I and type II cells since there are reasons to believe that the type I cells are innervated by thick fibers and the type II cells by thinner fibers. Brodal *et al.* (1962) found that primary vestibular fibers also reach the cerebellum where they could be followed to flocculus, nodulus and nucleus fastigii on the homolateral side.

d) Efferent fibers to the inner ear

The efferent fibers to the cochlea originate in the contralateral accessory superior olivary nucleus (Rasmussen, 1946, 1953) and in the ipsilateral superior olivary nucleus (Rasmussen, 1960). The ipsilateral portion passes posterior and lateral to the ascending part of the crossed main portion and unites with it lateral to the root fibers of the facial nerve. Approximately 3/4 of the fibers were reported to come from the contralateral side. Rasmussen described the efferent fibers to be myelinated, 3–5 μ thick and running as the olivocochlear bundle in the vestibular nerve. In the cat they were found to be about 500. However, since then Terayama *et al.* (1969) and Terayama and Yamamoto (1971) have shown that the olivocochlear bundle also contains unmyelinated fibers in both the crossed and uncrossed portions. The ratio of myelinated and unmyelinated fibers was said to be approximately 3:2.

The olivocochlear bundle leaves the vestibular nerve via the vestibulo-cochlear anastomosis of Oort and enters Rosenthal's canal where the fibers form intraganglionic spiral bundles. Rossi (1961) demonstrated AChE-positive fibers in the olivocochlear bundle, the intraganglionic spiral bundle and in the organ of Corti. Maw (1973) found terminals of myelinated fibers in the intraganglionic spiral bundle and a branching plexus of unmyelinated fibers. Wersäll (1956) reported two different types of nerve endings to the type II cells on the cristae, one containing more vesicles than the other. In Engström's (1958) work on the double innervation of the sensory epithelia of the inner ear two types of nerve endings were shown. One type had sparsely granulated nerve endings while those of the other type were richly granulated. It was assumed by Engström that the richly granulated endings were of an efferent nature and Engström and Fernandez (1961) showed that after transection of the crossed efferent bundle to the cochlea a majority of the efferent endings disappeared.

Schuknecht *et al.* (1959) using AChE-technique made degeneration studies and suggested that the crossed olivocochlear bundle fibers were continuous with the unmyelinated fibers and the nerve endings in the organ of Corti. It was demonstrated by Wersäll *et al.* (1961) and by Hilding and Wersäll (1962) that cholinesterase is closely related to the vesiculated nerve endings of cochlear and vestibular hair cells. Evidence of their efferent nature was provided by Iurato (1962) and by Kimura and Wersäll (1962).

With the AChE-technique Gacek *et al.* (1965) found a few, 20–30, efferent fibers running in the cochlear nerve trunk. These fibers were traced

towards the end organs of the upper middle and apical turns.

Petroff (1955) and Rasmussen and Gacek (1958) were the first to demonstrate an efferent fiber component of the vestibular nerve. The efferent fibers to the vestibular sensory regions seem to have their origin in the inferior region of the ipsilateral vestibular nuclear complex (Gacek, 1960, 1966). In the vestibular root and nerve these fibers run together with the efferent cochlear bundle as a compact bundle. Near the vestibular ganglion the vestibular efferents divide and run together with and scattered among the afferent fibers to the end organs (Gacek *et al.*, 1965). They reported the total number of myelinated efferent vestibular fibers to be about 400 in the cat.

e) Adrenergic innervation of the inner ear

The adrenergic innervation of the inner ear has been studied by a number of authors. Terayama *et al.* (1966), Terayama *et al.* (1968) were of the opinion that these fibers all came from the ipsilateral superior cervical ganglion and that they had a perivascular course along the arteries. Spoendlin and Lichtensteiger (1966) found apart from this perivascular system, also another and larger adrenergic system which consisted of fibers emerging in the central nervous system. These fibers reached the periphery via the cochlear nerve with the adrenergic fibers scattered among the afferent cochlear nerve fibers. This latter system is thus independent of the blood vessels and they reported it to form a peripheral plexus before the habenula perforata where the afferent fibers begin to become myelinated. In a following study Spoendlin and Lichtensteiger (1967) found the perivascular adrenergic system to be a continuous plexus around the vertebral, basilar, inferior anterior cerebellar and labyrinthine arteries reaching as far as the modiolar branches. The second, blood vessel independent system forms a rich terminal plexus in the area of the habenula perforata and below the vestibular sensory epithelia. Degeneration studies on cat indicated that these fibers originate in the superior cervical ganglion and reach the inner ear either via the tympanic plexus-facial nerve-internal auditory meatus or via the auricular branch of the vagus nerve-facial nerve and internal auditory meatus.

Ross (1971) also found a dual distribution of adrenergic fibers in the inner ear, one group was perivascular and the other went with the afferent cochlear fibers independently of blood vessels. It could not be clearly decided whether the two groups were of entirely separate origin. In this

study was also observed a bundle of adrenergic fibers that reached the inner ear via an anastomosis from the carotid plexus to the facial nerve along a course corresponding to the great superficial petrosal nerve. The blood vessel independent fibers occurred in greatest numbers within the osseous spiral lamina where some of the fibers formed arcades while others projected into the foramina nervosa where they ended as terminal beads.

The functional significance of an adrenergic system in the inner ear has not yet been clearly demonstrated. Spoendlin and Lichtensteiger (1966) speculated whether the adrenergic terminal plexus influences the action potential of the afferent system either by increasing or decreasing the discharge threshold. Ross (1971) proposed a generalized function for norepinephrine in influencing fluid balance and in modifying auditory nerve activity at the periphery.

4. Numerical studies of vestibular nerve fibers, ganglion cells, and sensory elements. Age related changes

Numerical studies of the vestibular nerve in man have been done by Rasmussen (1940), Bergström (1972) and Naufal and Schuknecht (1972).

Rasmussen counted the vestibular nerve fibers at an intracranial level and Naufal and Schuknecht sampled the vestibular ganglion cells. The distribution of nerve fibers to the different vestibular nerve branches could not be determined by either of these methods. Rasmussen divided his material into two groups; one from individuals 2 to 26 years old and the second from individuals 44 to 60 years old. In the first group he found between 15.300 and 24.000 vestibular nerve fibers with an average of 18.900. In the second group the number of nerve fibers ranged between 14.200 and 22.900 with an average of 18.000.

Naufal and Schuknecht found no age related variations in vestibular ganglion cell populations. They found an average number of 18.439 vestibular ganglion cells (range 14.920–22.390). However, they also reported an 86-year-old woman who had only 12.430 ganglion cells in the right and 10.910 in the left vestibular nerve but this reduction was attributed to diabetes mellitus which she had suffered from since the age of 40.

A caliber analysis by Engström and Rexed (1940) showed that the vestibular nerve fibers in general are thicker than the cochlear fibers. 88.5 % of the vestibular nerve fibers had an outer diameter between 2–8 μ , 7.2 % were thicker than 8 μ and 4.2 % thinner than 2 μ while in the cochlear nerve

77.1 % of the fibers had an outer diameter between 2–5 μ , 14.1 % 5–9 μ and 8.7 % were thinner than 2 μ . Rasmussen (1940) also found that the cochlear nerve fibers are thinner than the vestibular, in his study the cochlear fibers ranged from 3 to 10 μ with the majority 5–7 μ . The vestibular fibers varied from 2–15 μ , most of them were at least 10 μ thick.

The vestibular sensory cells have been analysed by Rosenhall (1972 a, 1972 b, 1973). In a group of individuals none of whom was older than 40 years, each of the three cristae had an average number of 7.600 hair cells (range 6.700–8.300). The macula utriculi contained 33.100 (29.500–39.200) hair cells and the macula sacculi 18.800 (16.000–21.300). In his material from old persons significant reductions in number of hair cells were found although great individual variations occurred. The cristae lost about 40 % of their hair cells on average and the maculae about 20 %.

Apart from Rosenhall's reports the existence of old age related degenerative changes in the vestibular system has been denied by a number of authors. v. Fieandt and Saxén (1937), Jørgensen (1964), Hansen and Reske-Nielsen (1964), Reske-Nielsen and Hansen (1964) have all studied the degenerative processes of the cochlea in aging. In that connection they also looked at the vestibular system without finding any changes that could be related to old age.

Schuknecht (1964) presented four cases with extensive degeneration in the cochlea attributed to old age. In one of the cases he reported degeneration of the macula sacculi while the rest of the vestibular system was said to be normal. In two of the cases the whole vestibular system was reported to be normal and in the fourth case there was no information about the vestibular part. Schuknecht *et al.* (1965) found what they called cochleo-saccular degeneration in an old cat, an old dog, and an old man. All these had extensive age related degeneration in the cochlea and losses of about 50 % of the hair cells of the macula sacculi. The other vestibular sensory regions appeared to be normal. They drew the conclusion that the phylogenetically younger pars inferior of the labyrinth is more vulnerable to aging than the phylogenetically older pars superior. Johnsson (1971) and Johnsson and Hawkins (1972 a) found age related degenerations in the macula sacculi but only minor changes in the macula utriculi. However, none of those reports was based on numerical studies. Sercer and Krmpotic (1958) and Krmpotic (1969) have found increasing bone apposition in the foramina for the cochlear and vestibular nerves and the fila olfactoria with

increasing age. They are of the opinion that these changes are the primary cause of presbycusis, presbystasis and presbyosmia and the nerve degenerations are of a secondary character.

C OBSERVATIONS

I. Anatomical studies of the vestibular nerve in man

The gross and topographical anatomy of the intratemporal part of the vestibular nerve in man was studied in 40 temporal bones. After decalcification the VIIIth and VIIth nerves and the inner ear were dissected. At the level of the vestibular ganglion the vestibular nerve divides into a superior and an inferior division. The superior division passes together with the facial nerve over the transverse crest in the fundus region of the internal auditory meatus and the inferior division and the cochlear nerve pass under this crest.

The superior division consists of the lateral and anterior ampullary nerves and the utricular nerve. The ampullary branches run as a unit for the greater part of their course and do not divide until just proximal to the respective ampullae. The utricular nerve is located immediately inferior to the ampullary branches.

The inferior division contains the saccular nerve and the posterior ampullary nerve. In one of the investigated nerve specimens the saccular nerve emitted two branches; one rather thick branch that passed over the transverse crest to the macula sacculi and one thinner branch which followed the main saccular nerve under the transverse crest. In practically all of the investigated nerves the posterior ampulla was innervated by two branches; the main posterior ampullary nerve and a thin accessory branch which usually left the vestibular nerve stem a little proximal and superior to the main branch. The topographical relationships between the vestibulo-cochlear and facial nerves and the inner ear are described.

A light microscopic study of the vestibular ganglion and the preganglionic part of the vestibular nerve was done on another 12 nerve specimens. The vestibular ganglion cells form one ganglion divided into a superior and an inferior portion connected by a narrow isthmus. The superior portion contains the ganglion cells of the neurons in the superior vestibular nerve division and the inferior portion those of the inferior division. When sectioned horizontally the superior portion of the ganglion has a more or less "Y"-shaped form with a maximum length of about 3 mm. The inferior portion is more elongated and slender and has a length of 4—4.5 mm. The isthmus region connects the proximal part of the superior portion with the central part of the inferior. The ganglion cells have a rich supply of small blood vessels. The ganglion cells are almost round or ovoid in form with

the nucleus more or less in the center. The diameters of the ganglion cells vary between 15 and 50 μ , the majority are 30–40 μ in diameter. Regional differences in cell size were not sufficiently evident to allow a subdivision of the ganglion based on the size of the ganglion cells.

II. The number of myelinated vestibular nerve fibers in man at various ages

This investigation was performed on the vestibular nerves from 11 individuals of varying ages ranging from birth to 85 years. There was no known history of vestibular disorders, such as Menière's disease or acoustic neuroma, or of treatment with ototoxic antibiotics or irradiation therapy to the head.

The aim of the study was twofold; (a) to establish the "normal" number of nerve fibers in the vestibular nerve and its branches and (b) to investigate whether any reduction in number occurs with increasing age.

The vestibular nerve fibers occur in bundles irregularly separated by connective tissue and blood vessels, therefore sampling procedures were not used and all fibers were counted. Control analyses without knowledge of the previous results differed less than 1 % from those.

The material was arranged in three groups according to age. The "young" or "normal" group consists of four individuals, 1 day to 35 years old. Two middle-aged persons, 49 and 53 years old constitute the second group. The third or "old age" group consists of five cases, 75–85 years old.

In the young group the number of myelinated vestibular nerve fibers ranged from 16.040 to 20.212 with an average of $18.346 \pm 3\%$. These results agree well with those of earlier reports. The distribution of nerve fibers in the different vestibular nerve branches has not been investigated earlier. In the present study the lateral and anterior ampullary nerves together contained an average number of 5.899 fibers, the utricular nerve, 5.952, the saccular nerve 4.046 and the posterior ampullary nerve 2.449 fibers. Two thirds of the vestibular nerve fibers are thus found in the superior division and one third in the inferior. Although the individual variations regarding the total number of myelinated vestibular nerve fibers are quite small the variations in the different nerve branches are pronounced.

The two middle-aged cases had 16.582 and 16.817 vestibular nerve fibers with an average of 16.700.

In the old age group the number of nerve fibers ranged between 9.274 and 15.980 with an average value of $11.506 \pm 7\%$. This reduction seemed to affect the ampullary and macular nerve fibers to about the same extent.

The reduction in number of the myelinated vestibular nerve fibers in the old age group averages 37 % when compared to the values of the young group. The reduction is statistically significant at better than the 1 % level.

III. Analysis of the calibers of the myelinated vestibular nerve fibers in man at various ages

The caliber spectra of the different vestibular nerve branches were analysed. The material consisted of nerve specimens from one newborn, four adults with "normal" or near-"normal" numbers of myelinated vestibular nerve fibers and four old persons with pronounced reductions in number of nerve fibers. These 9 cases were included in study II. The investigation was performed on cross sections from the preganglionic parts of the vestibular nerve branches. Photographs were taken through a photomicroscope and enlarged to 1000x magnification so that 1 mm on the photograph corresponded to 1μ in the specimen. At this magnification the outer diameters of the nerve fibers could be measured with accuracy. In all 10.210 fibers were analysed. The ampullary nerves and especially the two superior branches, were found to contain proportionally more thick fibers (6--15 μ) than the macular nerves.

In the newborn case the fibers were generally thinner than in the adult and old persons. In the old age group the proportion of thick fibers was less than in the adult group, especially in the ampullary nerve branches.

It could not be determined whether these changes were caused by disappearance of the thick fibers or were the result of a general involution of all nerve fibers in old age.

IV. Macula utriculi and macula sacculi in the squirrel monkey

This work contains an ultrastructural study of the vestibular nerve endings and the vestibular sensory cells. Practical and ethical considerations make it difficult to obtain human material suited for electron microscopical studies

of these regions and therefore the squirrel monkey which has an inner ear with a high degree of resemblance to the human inner ear (Spoendlin, 1965) was chosen for this study.

The vestibular sensory cells in the more highly developed species including man are of two types (Wersäll, 1956) characterized by their relations to the afferent nerve endings.

The phylogenetically younger type I cell is enclosed in a nerve chalice which is the terminal portion of a thick myelinated fiber. One nerve fiber can form separate chalices around a number of type I cells or it can form one larger chalice to enclose several type I cells. The nerve chalice has a wide area of contact towards the hair cell.

The type II cell receives several club shaped nerve endings which make synaptic contacts with the cell membrane in many regions mainly in the infranuclear but also in the supranuclear parts. The afferent nerve endings are sparsely granulated and contain rather large mitochondria.

Many different types of synaptic structures can be seen within the sensory cells. There are synaptic bars, bodies or balls and also many intermediate stages between these forms are found.

In the synaptic regions of afferent endings rich invaginations of a "coated type" can be observed. In some cases very long synaptic bars, sometimes more than 5 μ long, were observed. In certain regions of type I cells there is a tendency of a fusion in the synaptic membrane and the possibility of electric synapses must be further studied.

The efferent nerve endings are richly granulated and have smaller mitochondria than the afferent ones. The type I cells have no direct contact with the efferent nerve endings which usually are found near the "stem" of the nerve chalice. The efferent nerve endings to the type II cells will be found at many levels from the nucleus and downwards. Usually they are filled with round synaptic vesicles and inside the plasma membrane of the type II cell a subsynaptic cistern is often found.

The terminals of the efferent fibers were seen to run a complicated and richly branching course in the lower part of the sensory epithelium with good evidence of "en passant" synapses between efferent fibers both with sensory cells and with afferent fibers. They are readily recognized from afferent fibers because of the pronounced difference in the size of the mitochondria. It is thus directly possible to separate afferent and efferent fibers in the epithelium.

Inside the sensory epithelium the nerve fibers are unmyelinated. When they leave the sensory region a myelin sheath begins within a short distance

from the basement membrane. At this level the arrangement of the myelin layers around the axon with their complicated folds is evident.

Inside the sensory epithelium the afferent fibers to the type I cells are clearly thicker than those to the type II cells.

D. DISCUSSION

In the superior division of the vestibular nerve the branches to the anterior and lateral ampullae are almost inseparable during the greater part of their course. In a study on cat Gacek (1969) found that each of the two ampullary nerves was not associated with a distinct portion of the ganglion. He regarded them as one ampullary nerve which splits up peripherally to innervate two sensory areas. The posterior ampullary nerve was found to have a thin accessory branch in nearly all of the investigated cases. Montandon *et al.* (1970) reported two cases of crista neglecta in man where they observed an accessory branch to the posterior ampulla. This branch was said to leave the vestibular nerve stem distal to the main posterior ampullary nerve. They studied more than 600 temporal bones and in all of them two posterior ampullary nerves were found. In the present investigation the course of the nerve fibers inside the ampulla was not studied and no crista neglecta was seen.

The saccular nerve can occasionally emit one or two branches which also innervate the macula sacculi. The thick branch observed in one of the nerve specimens in the present material seems to be the same branch that Lindeman (1969) described while the thin branch in the same specimen probably is the cochleo-saccular nerve described by Hardy (1934) and Shute (1951).

The vestibular ganglion cells form one irregularly contoured ganglion divided into a pars superior and a pars inferior connected by a narrow isthmus. A few scattered ganglion cells were found outside the ganglion. It has a different form than the spiral ganglion which by Kellerhals *et al.* (1967) has been compared to a varicose chord. The vestibular ganglion cells are generally larger than the spiral ganglion cells and show greater variations regarding cell size (Alexander, 1899; Kellerhals *et al.*, 1967; Ballantyne and Engström, 1969).

It was not possible to make a reliable subdivision of the ganglion into specific regions based on the cell size as Lorente de Nó (1926) did in the rat.

The nerve specimens in the numerical study (II) were arranged in three age groups. The young or "normal" group included 4 cases, 1 day to 35 years old. This was in accordance with Rosenhall's observations that no significant sensory cell degenerations occurred before the age of 40. In the present study, however, a certain reduction in number of vestibular nerve fibers seems to have taken place already in the 35-year-old case but since

individual variations are likely to occur this case has been included in this group and not in the middle-aged group.

The average number of vestibular nerve fibers in this age group agree very well with those of Rasmussen (1940) and also with Naufal's and Schuknecht's results (1972).

In the old age group a significant reduction in number of nerve fibers was found. The average value 11.506 is 37 % less than that of the young group. Individual variations were found; a 75-year-old man thus had 15.980 fibers. The superior and inferior divisions of the vestibular nerve were equally affected and so were the saccular and posterior ampullary nerves. The superior division could not be reliably subdivided into ampullary and utricular branches in all cases in the old age group; any possible differences regarding the degree of reduction in the respective branches could therefore not be determined. In Rosenhall's studies the hair cells on the cristae suffered greater losses than those on the maculae.

In the same manner, as has long been known to occur in the acoustic part of the inner ear and VIIIth nerve, the vestibular parts undergo pronounced degenerations with increasing age. It thus seems as if with increasing age, and probably beginning around the age of 40, a general reduction of the number of sensory cells and their nerve fibers takes place.

Of great interest is that during the preparation of this paper, van der Laan (1972) of the Jongkees group has shown a reduction of vestibular sensitivity beginning at the age of 40.

It seems likely that elderly people can suffer from vestibular disorders due to degeneration of sensory cells and nerve fibers. The fact that vertigo and balance problems are common in old age is probably not caused by these peripheral lesions only but also by injuries to the central vestibular areas.

Clinical physiological studies have revealed age related changes in vestibular function (Arslan, 1957; Haas, 1964; Minnigerode *et al.*, 1967; Bruner and Norris, 1971; van der Laan, 1972). Possible explanations of the observed age effects were thought to be habituation, vascular influences and loss of central inhibition. van der Laan also suggested vestibular nerve degeneration as a possible cause. Vascular changes in the vessels of the internal auditory meatus and the inner ear with aging have been reported by Fisch *et al.*, (1972) and by Johnsson and Hawkins, (1972 b).

The ampullary nerves contain a greater proportion of thick fibers than the macular branches (III). It was also found that the myelinated fibers of the newborn boy were clearly thinner than those of the adult and old

individuals. Although the fibers of the 6-week-old boy (II) were not systematically measured they also appeared to be thinner than in the older cases. A gradual increase in size of the myelin sheath occurs during a long time after birth with increasing age (Westphal, 1897). The myelination of the vestibular nerve fibers begins at the 20th fetal week and is not completed until the time of puberty (Langworthy, 1933). In the old age group a deviation of the caliber spectra towards the thinner side was found, especially in the ampullary nerve branches.

A coarse estimation of the number of sensory cells innervated by each nerve fiber can be obtained by correlating the hair cell count in the different vestibular sensory regions with the number of nerve fibers in the nerve branches to these regions.

Lindeman (1969) estimated the number of hair cells in the different vestibular sensory regions in the guinea pig and Rasmussen and Gacek (1961) have analysed the number of vestibular nerve fibers in the same species. Their results are shown and correlated to each other in Tab. I. It is found that the hair cells on the ampullary cristae are supplied by relatively more nerve fibers than the macular hair cells, the average ratios being 3.3 sensory cells/nerve fiber for the two superior ampullae and 3.6 for the posterior ampulla while on the macula utriculi and macula sacculi there are 5.4 and 6.0 hair cells to each nerve fiber on average. The same correlation between the "normal numbers" of vestibular sensory cells in man reported by Rosenhall and the "normal numbers" of vestibular nerve fibers found in the present study is given in Tab. II. The average ratios are here 2.6 hair cells/nerve fiber for the two superior ampullae, 3.1 for the posterior ampulla and 5.6 and 4.6 cells to each nerve fiber for the macula utriculi and sacculi. The hair cells on the ampullary cristae thus seem to be relatively more richly innervated than those on the maculae in man also.

Table I.

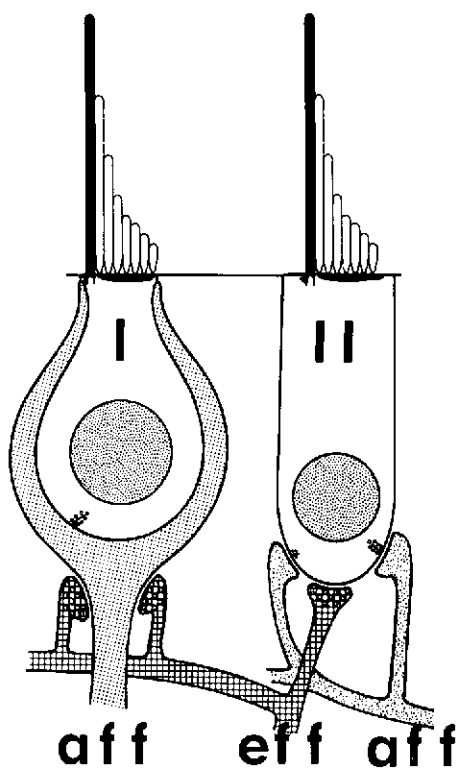
Correlation between sensory cells and nerve fibers in the guinea pig.

Guinea pig	Lindeman sens. cells	Gacek/Rasmussen nerve fibers	Ratio cells/fibers
amp ant et lat	11 130	3 389	3,3
mac utr	9 260	1 703	5,4
mac sacc	7 560	1 260	6,0
amp post	5 430	1 522	3,6

Table II.

Correlation between sensory cells and nerve fibers in man.

Man	Rosenhall sens. cells	Bergström nerve fibers	Ratio cells/fibers
amp ant et lat	15 200	5 899	2,6
mac utr	33 100	5 952	5,6
mac sacc	18 800	4 046	4,6
amp post	7 600	2 449	3,1

**Fig. 3.** Afferent (aff) and efferent (eff) innervation of hair cells type I and type II.

It is naturally not possible to determine exactly how many hair cells that each nerve fiber innervates, there are great variations so that one nerve fiber might innervate one or a few hair cells while another fiber is connected with several cells as can be seen in electron microscopic studies of the sensory regions (IV). The type I cell has only one afferent nerve ending but the type II cell has several. One type II cell can also receive nerve endings from several afferent fibers. It is possible but not probable that one nerve fiber gives off a number of nerve endings to a single type II cell. One type I and one type II cell can be innervated by the same nerve fiber and two or more type I cells can be supplied by a single fiber (Fig. 3).

The current information on the relations between type I and type II cells in the different vestibular regions is controversial (Lindeman, 1969; Watanuki *et al.*, 1971; Watanuki and Meyer zum Gottesberge, 1971). It is therefore at present not possible to draw any conclusions whether one cell type is relatively more richly innervated than the other.

The sensory cells on the cristae are innervated by proportionally more and thicker nerve fibers than the maculae. This should be of great functional importance and suggests higher demands on the cristae than on the maculae. It is also possible that faster reactions to angular than linear accelerations are required.

The intraepithelial portions of the fibers to the type I cells are thicker than those to the type II cells (IV). If the same caliber relations are present outside the sensory epithelium has not been possible to determine in this study. However, if so were the case it would indicate that the cristae contained relatively more type I cells than the maculae. It would also support the theories of Fernandez and coworkers (p. 15) that the regularly firing units correspond to fibers to type II cells and the irregular units correspond to thick fibers to type I cells.

E. SUMMARY

I. The gross and topographical anatomy of the intratemporal part of the vestibular nerve in man has been described. In nearly all of the examined temporal bones a thin accessory posterior ampullary nerve was seen to leave the vestibular nerve stem a little proximal to and above the main posterior ampullary nerve. This accessory branch was found to leave the internal auditory meatus through a separate foramen and it runs for a shorter or longer distance in its own bony canal before uniting with the main posterior ampullary nerve. In a few cases the two branches coursed separately all the way to the posterior ampulla.

The form and structure of the vestibular ganglion was studied with the light microscope. The vestibular ganglion cells form one ganglion divided into a superior and an inferior portion connected by a narrow isthmus. In the horizontal plane the superior portion is more or less "Y"-shaped while the inferior portion has a more elongated and slender form. It was not possible to subdivide the vestibular ganglion into specific regions based on the size of the ganglion cells.

The branches of the human vestibular nerve have been studied with reference to their general structure.

II. A numerical analysis of the vestibular nerve in individuals of varying ages has been done. In a group of young persons (not older than 35 years) the average number of myelinated vestibular nerve fibers was 18.346. The highest values (20.212 and 18.773) were found in a 6-week-old boy and in a newborn boy. The two superior ampullary nerves contained an average number of 5.899 fibers together, the utricular nerve 5.952, the saccular nerve 4.046 and the posterior ampullary nerve 2.449 fibers. The middle-aged cases showed a slight reduction in number of nerve fibers with an average value of 16.700 while in the old age group (75–85 years) a significant reduction down to an average value of only 11.506 fibers was found although individual variations occurred. Compared to the young group a loss of about 37 % of the myelinated vestibular nerve fibers was observed in the old age group.

These findings do not conform with earlier published reports in which age related degenerations of the peripheral vestibular system have been denied apart from the so called cochleo-saccular degeneration. They do, however, conform very well with recently found degenerations of the vestibular sensory regions in old age and also with a recent clinical study.

III. The caliber spectra of the myelinated fibers in the vestibular nerve branches were analysed in nerve specimens from individuals of various ages. The ampullary nerves contain a higher proportion of thick fibers than the macular nerves. In old age a deviation of the caliber spectra towards the thinner side occurs.

It was also found that the sensory cells on the cristae are relatively more richly innervated than those on the maculae.

IV. The peripheral endings of the vestibular nerve form a complicated pattern inside the vestibular sensory epithelia. In an electron microscopic study the intraepithelial portions of the afferent and efferent vestibular nerve fibers have been investigated. The squirrel monkey has been used for these experiments. As this animal is used to a great extent in our experimental work a careful study has been made not only of the nerves and nerve endings but also of the sensory epithelium. This is necessary for a better understanding of the synaptic morphology. A detailed description is given of the region of demyelination and of the intraepithelial course of the unmyelinated nerve fibers. The granulated or efferent fibers are very distinct from the afferent ones. They have much smaller and denser mitochondria and stand out very clearly (IV, Fig. 35).

The synaptic structures in the squirrel monkey vary considerably and sometimes very conspicuous synaptic bars as long as $5\ \mu$ can be seen. There are many different forms of synaptic structures and several types are demonstrated in this study.

The distance between nerve chalice and type I cell membrane was found to be in the order of $200\text{--}300\ \text{\AA}$ in the non-synaptic regions. In the synaptic regions the membranes are considerably closer to each other and sometimes the possibility of a real fusion must be considered. The distance between type II cell and afferent nerve endings was $123\ \text{\AA}$ on average in the synaptic region and the distance between the type II cell and the efferent nerve endings $161\ \text{\AA}$ on average.

The study also contains a detailed description of the sensory cells and their surface organelles. An interesting observation is that not only the sensory cells but also many supporting cells are provided with kinocilia. It is also shown that the cuticular plate is resting on a "shelf"-like reinforcement (IV, Figs. 20, 21, 22). It is further, among other observations, shown that the supporting cells contain a fine fibrillar reinforcement reaching from the basement membrane to the reticular membrane.

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